

REMARKS

Claims

Claims 1–5 and 9–10 are under examination with claims 6–8 and 11–17 withdrawn from consideration due to restriction/election. Claims 19–20 are added by this paper.

Claim amendments

Sub-claim (b) of Applicants' amended claim 1 incorporates the elements of claim 2, which is now cancelled. Support for sub-claim (d) can be found in the disclosure contained in, for example, page 9, ¶3 of the originally-filed specification. Support for the activity of the polypeptides that are encoded by the polynucleotides of the present invention can be found in, for example, page 8, lines 9–12 of the originally-filed specification and the disclosure contained in the Example.

Support for the amendment of claim 2 can be found in, for example, page 10, lines 6–8; the disclosure contained in the Examples and the sequence listing page of the instant specification.

Support for new claim 19 can be found in, for example, page 7, lines 1–26 of the originally-filed specification. New claim 20 is supported by the disclosure contained in, for example, page 31, lines 16–21 of the present specification.

It is submitted that the claim amendments do not add new matter.

Restriction/election

The restriction of claim 16, which is directed to polynucleotide molecules of the present invention, is incorrect. Inclusion of the claim into the examined claim set is respectfully requested.

Upon allowance of the generic product claims, Applicants reserve the right to request rejoinder of claims 11–15, which are drawn to a method of using the elected molecule(s) and/or composition(s). “If a product claim is found allowable, process claims that depend from or otherwise require all the limitations of the patentable product may be rejoined.” See M.P.E.P. § 806.05. See also, M.P.E.P. §821.04, “Rejoinder.”

Claim objections

The Examiner is thanked for her careful review of the claim listing. Correction has been

made with respect to the numbering of claims. The objection of claims 9 and 10, for allegedly reciting non-elected subject matter, is moot in view of the amendments.

Oath/declaration

The typographical error in the oath/declaration is noted. However, insofar as the application data sheet (ADS) filed herewith displays the correct information regarding the corresponding international application, the requirement for a new oath/declaration is misplaced. See, MPEP §601.05.

More specifically, 37 CFR §1.76(d) expressly outlines the provisions for correction of priority claim when there is an inconsistency between application data sheet and other documents.

37 CFR §1.76(d): Inconsistencies between application data sheet and other documents

- (1) The latest submitted information will govern notwithstanding whether supplied by an application data sheet, an amendment to the specification, a designation of a correspondence address, or by a §1.63 or §1.67 oath or declaration, except as provided by paragraph (d)(3) of this section;
- (2) The information in the application data sheet will govern when the inconsistent information is supplied at the same time by an amendment to the specification, a designation of correspondence address, or a §1.63 or §1.67 oath or declaration, except as provided by paragraph (d)(3) of this section;
- (3) The oath or declaration under §1.63 or §1.67 governs inconsistencies with the application data sheet in the naming of inventors (§ 1.41 (a)(1)) and setting forth their citizenship (35 U.S.C. 115);
(Emphasis added)

Withdrawal of the objection is respectfully requested.

Sequence Disclosure/Specification

Applicants are in the process of obtaining a revised sequence disclosure stating the origin of SEQ ID NO: 1 from a vendor specializing in such services. A revised specification and drawings, incorporating the sequence identifier numbers (SEQ ID NO) of all the biological sequences recited in the present application, is also being prepared by the vendor. Applicants will file a supplemental amendment to afford the PTO with these revisions. The Examiner is

respectfully requested to hold the objection of the specification and the drawings in abeyance until such can be obtained. See, MPEP 714.02 (b).

The abstract has been amended, rendering the objection thereof moot.

IDS

A copy of Klussman et al. is enclosed herewith, rendering the objection thereof moot.

Rejections under §112, ¶2

Applicants disagree that “multiple dependent phrase dependent on multiple dependent phrase” renders claim 1 indefinite. Sub-claims (a) through (c) of claim 1 are directed to polynucleotides having a recited sequence (i.e., SEQ ID NO: 1), variants thereof (80% homology to SEQ ID NO: 1) and degenerates thereof (i.e., degenerates of SEQ ID NO: 1 or degenerates of variants having 80% homology to SEQ ID NO: 1). Sub-claim (d), in its amended form, is directed to RNA equivalents of such polynucleotides.

The standard for definiteness under 35 U.S.C. §112, ¶2, is set forth in terms of reasonableness and in terms of consideration of both the prior art and the description provided in the application. Thus, the claims need not be absolutely definite but are acceptable when reasonably definite to one of ordinary skill in the art. See, for example, *In re Moore*, 439 F.2d 1232, 1235, 169 USPQ 236 (CCPA 1971); and, *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94-95 (Fed. Cir. 1986). As to both terms, the rejection appears to be based on the assertion that the terms are not limited to specifically defined structures and, thus, apparently, one of ordinary skill in the art would not find the terms reasonably definite. However, there is no assertion that one of ordinary skill in the art would not know the meaning of the terms “80% homology,” “degenerate” and “RNA.” Further, the Office Action appears to base the rejection, at least partly, on the assertion that the terms cover a large number of possible groups. However, the law does not support the proposition that breadth of a claim alone, is a proper basis for indefiniteness; see *In re Gardner*, 166 USPQ 138 (CCPA 1970) and M.P.E.P. §2173.04. Withdrawal of the rejection is respectfully requested.

Applicants disagree with the PTO’s contention that recitation of “functionally analogous” renders the claims indefinite. The claim term has been amended to recite “a behavior which is analogous to the AKAP188 polypeptide of SEQ ID NO: 2.” See, for example, page 8, lines 9–12 of the originally-filed specification for support. See also, new claim 20. Applicants’ amendment

of the claims is not to be construed as acquiescence to this or any other rejection.

The rejection of claim 1(a) under this section is moot in view of the amendments. However, Applicants respectfully disagree with the Office's contentions with regard to dependent claims 4, 9 and 10. Firstly, it is evident that the molecules recited in sub-claims (a) through (d) of claim 1 are all related to "*the polynucleotide sequence of SEQ ID NO: 1.*" Secondly, the claimed vectors, pharmaceutical preparations, and kits *may* comprise one or more nucleic acid types (for example, DNA or RNA) or polynucleotide sequences (for example, SEQ ID NO: 1 or variants thereof having 80% homology thereto). As stated *supra*, and further in view of a skilled worker's knowledge of molecular biology, these molecules are derivable from said SEQ ID NO: 1. As such, the alleged requirement that the claims be amended to recite "the polynucleotide" is misplaced. Withdrawal of the rejection is respectfully requested.

For the above reasons, it is urged that the instant claims are reasonably definite to one of ordinary skill in the art and, thus, the rejection under 35 U.S.C. §112, second paragraph, should be withdrawn.

Rejections under §102

The allegation that Trotter (*Journal of Cell Biology*, vol. 147, 1999) anticipates the claims of the present application is respectfully traversed.

The Office Action contends that "Trotter et al. teach a polynucleotide that has 69% homology to SEQ ID NO: 1." It is respectfully submitted that the rejection is moot in view of the amendment of the claims. For example, Trotter does not teach polynucleotides having at least 80% homology, degenerates thereof, or RNA equivalents thereof. Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. §112, ¶1 (written description)

Applicant has reviewed the PTO's *new Written Description Guidelines* and amended the claims in accordance with Example 11B beginning on Page 39 of the *Training Materials* (Rev. 1, March 25, 2008). While applicants may not agree with the agency's interpretation of the elements necessary to meet the statutory requirements of 35 U.S.C. § 112, ¶1, nonetheless, the pending claims have been amended to substantially conform to these.

The PTO's example provides a claim to a polynucleotide having the nucleic acid sequence of SEQ ID NO: 1, which encodes the polypeptide of SEQ ID NO: 2. The polypeptide of Serial No.: 10/526,768

SEQ ID NO: 2 has a novel activity Y. This conforms to Applicants' present invention wherein the claimed AKAP δ polynucleotide of SEQ ID NO: 1 encodes a protein of SEQ ID NO: 2 which has a novel activity (for example, AKAP δ protein anchors protein kinase A (PKA) with Ca $^{2+}$ channels or receptors in cells, as recited in present claim 20). The exemplary claims are as follows:

Claim 1. An isolated nucleic acid that encodes a polypeptide with at least 85% amino acid sequence identity to SEQ ID NO: 2.

Claim 2. An isolated nucleic acid that encodes a polypeptide with at least 85% amino acid sequence identity to SEQ ID NO: 2; wherein the polypeptide has activity Y.

The guidelines state that both claims 1 and 2 satisfy the requirements set forth under §112, ¶1. With respect to claim 1, it is stated that "Although the recitation of a polypeptide with at least 85% identity represents a partial structure...the disclosure of SEQ ID NO: 2 combined with the knowledge in the art regarding the genetic code would put one in possession of the genus of nucleic acids that encode SEQ ID NO: 2. Further, with the aid of a computer, one could list all of the nucleic acid sequences that encode a polypeptide with at least 85% sequence identity with SEQ ID NO: 2. Additionally, the level of skill and knowledge in the art is such that one of ordinary skill would be able to use conventional sequencing and nucleic acid synthesis techniques to routinely generate and identify nucleic acids that encode the polypeptide of SEQ ID NO: 2, as well as those that encode any polypeptide having 85% structural identity to SEQ ID NO: 2. Thus, one of ordinary skill in the art conclude that the applicant would have been in possession of the claimed genus at the time of filing."

With respect to claim 2, it is stated that "[although] the specification fails to teach which of the nucleic acid sequences that encode a polypeptide with at least 85% sequence identity to SEQ ID NO: 2 encode a polypeptide having the required activity Y,... the specification identifies domains responsible for activity Y." Such a disclosure is evident from the disclosure contained in Applicants' specification. For example, the present specification discloses at least three types of AKAP proteins, AKAP18, AKAP δ and AKAP η , and provides information relating to the primary structure (i.e., polypeptide sequence) and function of all three members. See, for example, the paragraph bridging pages 8 and 9; the disclosure contained in the "Results" section at page 27. The cited art by Trotter (*Journal of Cell Biology*, vol. 147, 1999), provides information on yet another member of this protein family.

The guidelines further states that "Although all conservative amino acid substitutions in Serial No.: 10/526,768 -11- HERTIN-0001

these domains will not necessarily result in a protein having activity Y, those of ordinary skill in the art would expect that many of these conservative substitutions would result in a protein having the required activity. Thus, a correlation exists between the function of the claimed protein and the structure of the disclosed binding and catalytic domains [such that] based on the applicant's disclosure and the knowledge within the art, those of ordinary skill in the art would conclude that the applicant would have been in possession of the claimed genus of nucleic acids based on the disclosure of the single species of SEQ ID NO: 1."

Thus, it is evident that the specification clearly provides the information set forth by the U.S. Patent Office as needed to meet the statutory requirements under §112, ¶1. Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. §112, ¶1 (enablement)

Regarding the lack of enablement rejection of claim 1, Applicants courteously submit that the specification, coupled with a skilled worker's knowledge, provides adequate guidance to make and use the polynucleotides and polypeptides of the instant invention. "To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' *Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993)). For example, the present application provides polypeptide sequences (SEQ ID NO: 2 and/or homologs thereof). Methods of obtaining other polypeptide/polynucleotide sequences are also described. See, for example, the disclosure contained in pages 24-26 of the instant application and the information provided in the sequence listing. Methods of making and preparing the AKAP18δ polypeptides of the instant invention are provided. These include recombinant techniques (as exemplified) as well as chemical synthetic means that are known in the art. Polypeptides *comprising* a polypeptide having the polypeptide sequence of SEQ ID NO: 2, for example, fusion proteins comprising at least one of SEQ ID NO: 2 are also described. See, the disclosure on the CFP-tagged AKAP18δ proteins. The utility of such fusion proteins, for example, in cytological studies, is further outlined in the Examples.

Variant polypeptides which are encoded by polynucleotide sequences that share, for example, 80% homology with SEQ ID NO: 1 could be routinely generated via synthesis and design of DNA constructs and/or vectors that encode such polypeptides. Such techniques were known in the art. In accordance with Applicants' own disclosure, the skilled worker could utilize known techniques (for example, conserved substitutions) to generate polynucleotides that share at

least 80% homology with SEQ ID NO: 1, transform a host cell (for example, eukaryotic cell) with the variant polynucleotide sequence, thus generating a repertoire of polypeptide molecules. These variant polypeptides could then be routinely tested with regard to their ability to bind to protein kinase A regulatory subunit II, for example, using the assays described in Applicants' own specification. See, page 27, line 28 to page 33, line 10 of the originally-filed specification. Thus a genus of molecules which satisfy the claimed structural and/or functional elements can be isolated and tested. The whole process would constitute nothing more than routineness.

In light of this detailed disclosure, the courts have placed the burden on the PTO to show otherwise. It is courteously submitted that the Examiner has not presented any evidence to refute the findings or the conclusions made herein. In addition, no evidence has been presented to support the contention that the claimed compounds could not be made and used, in a manner that is commensurate with Applicants' claimed invention. Only unsupported allegations and conclusions regarding the "complexity" and "unpredictability" of the "broad genus" are provided. These are especially weak in the face of the showing that the state of the art pertaining to polypeptide molecules of the present invention, protein formulations, and use of such molecules in therapeutics are all mature.

Applicants further invite the Examiner to review a recent precedential opinion issued by the United States Board of Patent Appeals and Interferences (*Ex parte* Kubin, B.A.P.I. 2007), a copy of which is enclosed herewith.

The facts in Kubin are applicable to the present case. In Kubin, the Examiner contended that "at least 80% identity language" in the absence of any working examples, other than a few representative species, fails to provide enablement of the claimed genus of molecules. See, page 10 of *Ex parte* Kubin. The Examiner alleged that specification did not teach "which 20% . . . of amino acid residues should be changed in order to maintain the biological functions." In response, Appellants argued that the specification disclosed "in detail how to: 1) make variants of SEQ ID NOs: 1 and 2; 2) calculate the percent identity between SEQ ID NOs: 1 and 2 and the variant sequence; and 3) test the variant sequence to determine [functional activity]." See, items 23 and 24 at page 13. Appellants further argued that in view of the high level of skill in molecular biology, methods of making the claimed nucleic acid sequences and screening for activity [were] known in the art and described in the specification and that the "experimentation involved to produce other sequences within the scope of the claims" and thus to practice the full scope of the claims would have been "well within the skill of those in the art." The amount of

experimentation involved would have been routine and not undue. See, items 27–30 at page 14.

The Board of Patent Appeals and Interferences in reversing the enablement rejection concluded:

“The amount of experimentation to practice the full scope of the claimed invention might have been extensive, but it would have been routine. The techniques necessary to do so were well known to those skilled in the art. *See, e.g., Johns Hopkins Univ. v. Cellpro, Inc.*, 152 F.3d 1342, 1360, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998) (“test [for undue experimentation] is not merely quantitative . . . if it is merely routine.”). A “patent need not teach, and preferably omits, what is well known in the art.” *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986). Thus, we conclude the Specification would have enabled the full scope of claim 73. (Emphasis added)

Likewise in the present application, Applicants disclose a genus of AKAP18 δ polynucleotides having a disclosed sequence and polypeptides encoded therefrom. Methods of obtaining other polynucleotide sequences, for example, polynucleotides which are 80% homologous to SEQ ID NO: 1, were all routine. As discussed *supra*, such techniques may involve the use of a computer or other biochemical means. For example, variant nucleic acid sequences could be generated via site-specific mutagenesis of SEQ ID NO: 1. Specific hybridization techniques may also be used to isolate these variant polynucleotide sequences. *See, complete paragraphs 8 and 9 at page 7 of the instant specification.* A skilled artisan could routinely utilize translation techniques for identifying polypeptides which are encoded by such variant polynucleotides (for example, using translation tools) and whether such polypeptides would meet the structural features of AKAP18 δ proteins. Polynucleotides which encode such proteins could then be expressed and assayed for claimed activity using art-known techniques, for example, binding assays and/or FRET-based studies. *See, for example, the disclosure contained in Example of the present application.* Therefore, the level of “experimentation involved to produce other sequences within the scope of the claims” and thus to practice the full scope of the claims would have been “well within the skill of those in the art.”

In view of the above remarks, it is respectfully submitted that Applicants' disclosure provides more than sufficient guidance to objectively enable one of ordinary skill in the art to make and use the claimed invention with an effort that is routine with in the art. Withdrawal of the rejection under 35 U.S.C. §112, ¶1, is respectfully requested.

If there are any remaining issues which can be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

No fees are believed to be due with this response; however, the Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

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Encl.

- o *Ex parte* Kubit, B.A.P.I. 2007
- o Klussman et al.